

SEQUENCE LISTING

<110> Von der Muelbe, Florian
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Pascolo, Steve (nur US)

<120> Pharmazeutische Zusammensetzung, enthaltend eine
stabilisierte und für die Translation in ihren
codierenden Bereichen optimierte mRNA

<130> CU01P003WO

<140> PCT/EP02/06180

<141> 2002-06-05

<160> 13

<170> PatentIn Ver. 2.1

<210> 1

<211> 774

<212> DNA

<213> Influenza virus

<220>

<223> Influenza-Matrix: Wildtyp-Gen (zum Vergleich)

<220>

<223> Startcodon: atg (Nucleotide 11 bis 13), Stopcodon:
tga (Nucleotide 767 bis 769)

<400> 1

```

agatctaaag atgagtccttc taaccgaggt cgaaacgtac gttctctcta tcatcccgtc 60
agggcccttc aaagccgaga tcgcacagag acttgaagat gtctttgcag ggaagaacac 120
cgatcttgag gttctcatgg aatggctaaa gacaagacca atcctgtcac ctctgactaa 180
ggggatttta ggatttgtgt tcacgctcac cgtgccaggt gagcgaggac tgcagcgtag 240
acgctttgtc caaaatgccc ttaatgggaa cggggatcca aataacatgg acaaagcagt 300
taaaactgtat aggaagctca agagggagat aacattccat ggggccaaag aaatctcact 360
cagttattct gctggtgcac ttgccagttg tatgggcctc atatacaaca ggatgggggc 420
tgtgaccact gaagtggcat ttggcctggg atgtgcaacc tgtgaacaga ttgctgactc 480
ccagcatcgg tctcataggc aaatgggtgac aacaaccaac ccactaatca gacatgagaa 540
cagaatgggt ttagccagca ctacagctaa ggctatggag caaatggctg gatcgagtga 600
gcaagcagca gaggccatgg aggttgctag tcaggctagg caaatgggtc aagcgatgag 660
aaccattggg actcatccta gctccagtgc tggctgaaa aatgatcttc ttgaaaattt 720
gcaggcctat cagaaacgaa tgggggtgca gatgcaacgg ttcaagtga ctag 774

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<210> 2

<211> 252

<212> PRT

<213> Influenza virus

<400> 2

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Met Ser Leu Leu Thr Glu Val Glu Thr Tyr Val Leu Ser Ile Ile Pro
  1              5              10              15

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Ser Gly Pro Leu Lys Ala Glu Ile Ala Gln Arg Leu Glu Asp Val Phe
      20              25              30

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Ala Gly Lys Asn Thr Asp Leu Glu Val Leu Met Glu Trp Leu Lys Thr
  35              40              45

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Arg Pro Ile Leu Ser Pro Leu Thr Lys Gly Ile Leu Gly Phe Val Phe

```

50	55	60
Thr Leu Thr Val Pro Ser Glu Arg Gly Leu Gln Arg Arg Arg Phe Val		
65	70	75 80
Gln Asn Ala Leu Asn Gly Asn Gly Asp Pro Asn Asn Met Asp Lys Ala		
	85	90 95
Val Lys Leu Tyr Arg Lys Leu Lys Arg Glu Ile Thr Phe His Gly Ala		
	100	105 110
Lys Glu Ile Ser Leu Ser Tyr Ser Ala Gly Ala Leu Ala Ser Cys Met		
	115	120 125
Gly Leu Ile Tyr Asn Arg Met Gly Ala Val Thr Thr Glu Val Ala Phe		
	130	135 140
Gly Leu Val Cys Ala Thr Cys Glu Gln Ile Ala Asp Ser Gln His Arg		
	145	150 155 160
Ser His Arg Gln Met Val Thr Thr Thr Asn Pro Leu Ile Arg His Glu		
	165	170 175
Asn Arg Met Val Leu Ala Ser Thr Thr Ala Lys Ala Met Glu Gln Met		
	180	185 190
Ala Gly Ser Ser Glu Gln Ala Ala Glu Ala Met Glu Val Ala Ser Gln		
	195	200 205
Ala Arg Gln Met Val Gln Ala Met Arg Thr Ile Gly Thr His Pro Ser		
	210	215 220
Ser Ser Ala Gly Leu Lys Asn Asp Leu Leu Glu Asn Leu Gln Ala Tyr		
	225	230 235 240
Gln Lys Arg Met Gly Val Gln Met Gln Arg Phe Lys		
	245	250

<210> 3
 <211> 775
 <212> DNA
 <213> Artificial Sequence

<220>
 <223> Description of Artificial Sequence:
 Influenza-Matrix: Gen mit erhöhtem G/C-Gehalt

<220>
 <223> Startcodon: atg (Nucleotide 11 bis 13), Stopcodon:
 tga (Nucleotide 767 bis 769):

<400> 3
 agatctaaag atgagcctgc tgaccgaggt ggagacctac gtgctgagca tcatccccag 60
 cgcccccttg aaggccgaga tcgcccagag gctggaggac gtgttcgccg gcaagaacac 120
 cgacctggag gtgctgatgg agtggctgaa gaccaggccc atcctgagcc ccctgaccaa 180
 gggcctcctg ggcttcgtgt tcacctgac cgtgcccagc ggcgcggcc tgcagcgccg 240
 ccgcttcgtg cagaacgccc tgaacggcaa cggcgacccc aacaacatgg acaaggccgt 300
 gaagctgtac aggaagctga agagggagat caccttcac ggcgccaagg agatcagcct 360
 gagctacagc gccggcgccc tggccagctg catgggcctg atctacaaca ggatgggcgc 420
 cgtgaccacc gaggtggcct tcggcctggt gtgcgccacc tgcgagcaga tcgccgacag 480
 ccagcaccgc agccacaggc agatggtgac caccaccaac cccctgatca ggcacgagaa 540
 caggatggtg ctggccagca ccaccgcaa ggccatggag cagatggccg gcagcagcga 600

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gcaggccgcc gaggccatgg aggtggccag ccaggccagg cagatggtgc aggccatgag 660
gaccatcggc acccacccca gcagcagcgc cggcctgaag aacgacctgc tggagaacct 720
gcaggcctac cagaagcgca tgggcgtgca gatgcagcgc ttcaagtga ctagt 775
```

<210> 4
 <211> 844
 <212> DNA
 <213> Artificial Sequence

<220>
 <223> Description of Artificial Sequence:
 Influenza-Matrix: Gen für sekretierte Form (mit
 N-terminaler Signalsequenz) mit erhöhtem
 G/C-Gehalt

<220>
 <223> Startcodon: atg (Nucleotide 11 bis 13), Stopcodon:
 tga (Nucleotide 836 bis 838)

```
<400> 4
agatctaaag atggccgtca tggccccccg caccctggtg ctgctgctga gggcgccct 60
ggccctgacc cagacctggg ctagcctgct gaccgaggtg gagacctacg tgctgagcat 120
catccccagc ggccccctga aggccgagat cgcccagagg ctggaggacg tgttcgcccg 180
caagaacacc gacctggagg tgctgatgga gtggctgaag accaggccca tcctgagccc 240
cctgaccaag ggcacccctg gcttcgtggt caccctgacc gtgcccagcg agcgcgccct 300
gcagcgccgc cgcttcgtgc agaacgccct gaacggcaac ggcgacccca acaacatgga 360
caaggccgtg aagctgtaca ggaagctgaa gagggagatc accttccacg gcgccaagga 420
gatcagcctg agctacagcg ccggcgccct ggccagctgc atgggcctga tctacaacag 480
gatgggcgcc gtgaccaccg aggtggcctt cggcctggtg tgcgccacct gcgagcagat 540
cgccgacagc cagcaccgca gccacaggca gatggtgacc accaccaacc ccctgatcag 600
gcacgagaac aggatggtgc tggccagcac caccgccaa gcatggagc agatggcccg 660
cagcagcgag caggccgccg aggccatgga ggtggccagc caggccaggc agatggtgca 720
ggccatgagg accatcgcca cccaccccag cagcagcgcc ggcctgaaga acgacctgct 780
ggagaacctg caggcctacc agaagcgcat gggcgtgcag atgcagcgct tcaagtgaac 840
tagt 844
```

<210> 5
 <211> 942
 <212> RNA
 <213> Artificial Sequence

<220>
 <223> Description of Artificial Sequence:
 Influenza-Matrix: mRNA mit
 Stabilisierungssequenzen

<220>
 <223> Die Stabilisierungssequenzen stammen aus den 5'-
 bzw. 3'-UTRs der β -Globin-mRNA von *Xenopus laevis*

<220>
 <223> Startcodon: aug (Nucleotide 56 bis 58), Stopcodon:
 uga (Nucleotide 812 bis 814)

```
<400> 5
gcuuguucuu uuugcagaag cucagaauaa acgcucaacu uuggcagauc uaaagaugag 60
ucuucuaacc gaggucaaaa cguacguucu cucuaucauc ccgucaggcc ccucaaagc 120
cgagaucgca cagagacuug aagaugucuu ugcagggaag aacaccgauc uugagguucu 180
cauggaaugg cuaaagacaa gaccaauccu gucaccucug acuaagggga uuuuaggauu 240
uguguucacg cucaccgugc ccagugagcg aggacugcag cguagacgcu uuguccaaaa 300
ugcccuuaau gggaacgggg auccaaauaa cauggacaaa gcaguuaaac uguauaggaa 360
```

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gcucaagagg gagauaacau uccauggggc caaagaaauc ucacucaguu auucugcugg 420
ugcacuugcc aguuguauagg gccucauaau caacaggau ggggcuguga ccacugaagu 480
ggcauuuggc cugguauugug caaccuguga acagauugcu gacucccagc aucggucuca 540
uaggcaaaug gugacaacaa ccaacccacu aaucagacau gagaacagaa ugguuuuagc 600
cagcacuaca gcuaaggcua uggagcaaa uggcuggaucg agugagcaag cagcagaggc 660
cauggagguu gcuagucagg cuaggcaaa ugggcaagcg augagaacca uggggacuca 720
uccuagcucc agugcugguc ugaaaaauga ucuucugaa aauuugcagg ccuauacagaa 780
acgaaugggg gugcagaugc aacgguucaa gugaacuagu gacugacuag cccgcugggc 840
cucccaacgg gccuccucc ccuccuugca ccaaaaaaaaa aaaaaaaaaa aaaaaaaaaa 900
aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aa 942

```

```

<210> 6
<211> 942
<212> RNA
<213> Artificial Sequence

```

```

<220>
<223> Description of Artificial Sequence:
      Influenza-Matrix: mRNA mit erhöhtem G/C-Gehalt und
      Stabilisierungssequenzen

```

```

<220>
<223> Die Stabilisierungssequenzen stammen aus den 5'-
      bzw. 3'-UTRs der  $\beta$ -Globin-mRNA von Xenopus laevis

```

```

<220>
<223> Startcodon: aug (Nucleotide 56 bis 58), Stopcodon:
      uga (Nucleotide 812 bis 814)

```

```

<400> 6
gcuuguucuu uuugcagaag cucagaauaa acgcucaacu uuggcagau uaaagaugag 60
ccugcugacc gagguggaga ccuacgugcu gagcaucauc cccagcggcc ccugaaggc 120
cgagaucgcc cagaggcugg aggacguguu cgccggcaag aacaccgacc uggaggugcu 180
gauggagugg cugaagacca ggcccauccu gagccccug accaagggca uccugggcuu 240
cguguucacc cugaccgugc ccagcgagcg cggccugcag cgccgccgcu ucgugcagaa 300
cgcccuagaac ggcaacggcg accccaacaa cauggacaag gccgugaagc uguacaggaa 360
gcugaagagg gagauaccu uccacggcgc caaggagau agccugagcu acagcgccgg 420
cgccugggc agcugcaugg gccugaucua caacaggau ggcgcguga ccaccgaggu 480
ggccuucggc cuggugugcg ccaccugcga gcagaucgcc gacagccagc accgcagcca 540
caggcagaug gugaccacca ccaaccccu gaucaggcac gagaacagga uggugcuggc 600
cagcaccacc gccaggcca uggagcagau ggccggcagc agcgagcagg ccgccaggc 660
cauggaggug gccagccagg ccaggcagau ggugcaggcc augaggacca ucggcaccca 720
ccccagcagc agcgccggcc ugaagaacga ccugcuggag aaccugcagg ccuaccagaa 780
gcgaugggc gugcagaugc agcgcuucaa gugaacuagu gacugacuag cccgcugggc 840
cucccaacgg gccuccucc ccuccuugca ccaaaaaaaaa aaaaaaaaaa aaaaaaaaaa 900
aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aa 942

```

```

<210> 7
<211> 1011
<212> RNA
<213> Artificial Sequence

```

```

<220>
<223> Description of Artificial Sequence:
      Influenza-Matrix: für sekretierte Form codierende
      mRNA mit erhöhtem G/C-Gehalt und
      Stabilisierungssequenzen

```

```

<220>
<223> Startcodon: aug (Nucleotide 56 bis 58), Stopcodon:
      uga (Nucleotide 881 bis 883)

```

```

<400> 7
gcuuguucuu uuugcagaag cucagaaaua acgcucaacu uuggcagauc uaaagauggc 60
cgucaaggcc ccccgacccc uggugcugcu gcugagcggc gccugggccc ugacccagac 120
cuggggccagc cugcugaccg aggguggagac cuacgugcug agcaucaucc ccagcggccc 180
ccugaaggcc gagaucgccc agaggcugga ggauguguuc gccggcaaga acaccgaccu 240
ggaggugcug auggaguggc ugaagaccag gcccauccug agccccuga ccaagggaau 300
ccugggcuuc gugucacccc ugaccgugcc cagcgagcgc ggcugcagc gccgccgcuu 360
cgugcagaac gcccugaacg gcaacggcga cccaacaac auggacaagg ccgugaagcu 420
guacaggaag cugaagaggg agaucaccuu ccacggcgcc aaggagauca gccugagcua 480
cagcgccggc gcccuggcca gcugcauggg ccugaucuaa aacaggauug gcgccgugac 540
caccgaggug gccuucggcc uggugugcgc caccugcgag cagaucgccg acagccagca 600
ccgcagccac aggcagaugg ugaccaccac caacccccug aucaggcacg agaacaggau 660
ggugcuggcc agcaccaccg ccaaggccau ggagcagaug gccggcagca gcgagcaggc 720
cgccgaggcc auggaggugg ccagccaggc caggcagaug gugcaggcca ugaggaccu 780
cggcaccac cccagcagca gcgccggccu gaagaacgac cugcuggaga accugcaggc 840
cuaccagaag cgcaugggcg ugcagaugca gcgcuucaag ugaacuagug acugacuagc 900
ccgcugggcc ucccaacggg ccuuccucc cuccuugcac caaaaaaaaa aaaaaaaaaa 960
aaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa a 1011

```

```

<210> 8
<211> 940
<212> DNA
<213> Homo sapiens

```

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<220>
<223> MAGE1: Wildtyp-Gen (zum Vergleich)

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<220>
<223> Startcodon: atg (Nucleotide 5 bis 7), Stopcodon:
tga (Nucleotide 932 bis 934)

```

```

<400> 8
catcatgtct cttgagcaga ggagtctgca ctgcaagcct gaggaagccc ttgaggccca 60
acaagaggcc ctgggcctgg tgtgtgtgca ggctgccacc tcctcctcct ctccctctggt 120
cctgggcacc ctggaggagg tgcccactgc tgggtcaaca gatcctcccc agagtcttca 180
gggagcctcc gcctttccca ctaccatcaa cttcactega cagaggcaac ccagtgaggg 240
ttccagcagc cgtgaagagg aggggccaag cacctcttgt atcctggagt ccttggtccg 300
agcagtaatc actaagaagg tggctgattt ggttggtttt ctgctcctca aatatcgagc 360
cagggagcca gtcacaaagg cagaaatgct ggagagtgtc atcaaaaatt acaagcactg 420
ttttcctgag atcttcggca aagcctctga gtccttgag ctggtctttg gcattgacgt 480
gaaggaagca gacccaccg gccactccta tgtccttgct acctgcctag gtctctccta 540
tgatggcctg ctgggtgata atcagatcat gcccaagaca ggcttcctga taattgtcct 600
ggtcatgatt gcaatggagg gcggccatgc tcctgaggag gaaatctggg aggagctgag 660
tgtgatggag gtgtatgatg ggagggagca cagtgcctat ggggagccca ggaagctgct 720
cacccaagat ttggtgcagg aaaagtacct ggagtaccgg caggtgccgg acagtgatcc 780
cgcacgctat gagttcctgt ggggtccaag ggcctcgtc gaaaccagct atgtgaaagt 840
ccttgagtat gtgatcaagg tcagtgaag agttcgcttt ttcttcccat cctgcgtga 900
agcagctttg agagaggagg aagagggagt ctgagcatga 940

```

```

<210> 9
<211> 308
<212> PRT
<213> Homo sapiens

```

```

<220>
<223> Tumorantigen MAGE1: Proteinsequenz

```

```

<400> 9
Ser Leu Glu Gln Arg Ser Leu His Cys Lys Pro Glu Glu Ala Leu Glu
1 5 10 15

```


<220>

<223> Description of Artificial Sequence: MAGE1: mRNA
mit erhöhtem G/C-Gehalt

<220>

<223> Startcodon: aug (Nucleotide 1 bis 3), Stopcodon:
uga (Nucleotide 937 bis 939)

<400> 10

```
augagccugg agcagcgcag ccugcacugc aagccggagg aggcgcugga ggcgagcag 60
gaggcgugg gccuggucug cguccaggcg ggcagagca gcagagccc gcugguccug 120
ggcagcugg aggaggucc gacggcgggc agcacggacc cgccgcagag cccgcagggc 180
gcgagcgcu ucccgacgac gaucaacuuc acgcgccagc gccagccgag cgagggcagc 240
agcagccgcg aggaggagg cccgagcacg agcugcaucc uggagagccu guuccgcgcg 300
gucaucacga agaaggucgc ggaccugguc ggcuccugc ugcugaagua ccgcgcgcgc 360
gagccgguca cgaaggcgga gaugcuggag agcgucauca agaacuacaa gcacugcuuc 420
ccggagaucu ucggcaaggc gagcgagagc cugcagcugg ucuucggcau cgacgucaag 480
gaggcgacc cgacgggcca cagcuacguc cuggucacgu gccugggccu gagcuacgac 540
ggccugcugg ggcacaacca gaucaugccg aagacgggcu uccugaucau cguccugguc 600
augagcgca uggaggcgcg ccacgcgccg gaggaggaga ucugggagga gcugagcguc 660
auggaggucu acgacggcgg cgagcacagc gcuacggcg agccgcgcaa gcugcugacg 720
caggaccugg uccaggagaa guaccuggag uaccgccagg ucccgacag cgacccggcg 780
cgcuacgagu uccugugggg cccgcgcgcg cuggccgaga cgagcuacgu caagguccug 840
gaguacguga ucaaggucag cgcgcgcguc cgcuucuucu ucccagagccu gcgcgaggcg 900
gcgcugcgcg aggaggagga gggcgucuga gcgugauga 939
```

<210> 11

<211> 939

<212> RNA

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: MAGE1: mRNA
mit alternativer Codonverwendung

<220>

<223> Startcodon: aug (Nucleotide 1 bis 3), Stopcodon:
uga (Nucleotide 937 bis 939)

<400> 11

```
augagccugg agcagcgcag ccugcacugc aagcccagg aggccugga ggcccagcag 60
gaggcccugg gccuggugug cgugcaggcc gccaccagca gcagagccc ccuggugcug 120
ggcaccugg aggagugucc caccgccggc agcaccgacc cccccagag ccccagggc 180
gccagcgccu ucccaccac caucaacuuc acccgccagc gccagcccag cgagggcagc 240
agcagccgcg aggaggagg ccccagcacc agcugcaucc uggagagccu guuccgcgcc 300
gugaucacca agaagguggc cgaccuggug ggcuccugc ugcugaagua ccgcgccgc 360
gagcccguga ccaaggccga gaugcuggag agcgugaucaga agaacuacaa gcacugcuuc 420
cccgagaucu ucggcaaggc cagcgagagc cugcagcugg uguucggcau cgacgugaag 480
gaggccgacc ccaccggcca cagcuacguc cuggugaccu gccugggccu gagcuacgac 540
ggccugcugg ggcacaacca gaucaugccc aagaccggcu uccugaucau cgugcuggug 600
augaucgcca uggaggcgcg ccacgcccc gaggaggaga ucugggagga gcugagcgug 660
auggaggugu acgacggcgg cgagcacagc gccuacggcg agcccgcaa gcugcugacc 720
caggaccugg ugcaggagaa guaccuggag uaccgccagg ugcccagacag cgaccccgcc 780
cgcuacgagu uccugugggg ccccgcgcc cuggccgaga ccagcuacgu gaaggugcug 840
gaguacguga ucaaggugag cgcccgcgug cgcuucuucu ucccagagccu gcgcgaggcc 900
ggccugcgcg aggaggagga gggcguguga gccugauga 939
```

<210> 12

<211> 7

<212> RNA

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Ein für eine
Endonuklease erkennbares Sequenzmotiv, das im
3'UTR-Segment des für den Transferin-Rezeptor
codierenden Gens enthalten ist (S. 10 der
Beschreibung).

<400> 12

gaacaag

7

<210> 13

<211> 13

<212> RNA

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Kozak-Sequenz,
Ribosomen-Bindungsstelle (S. 12 der Beschreibung)

<400> 13

gccgccacca ugg

13